

## Bitot's Spots and Vitamin A Deficiency

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Nearly 100 years have elapsed since the French physician, Bitot, described the conjunctival spots which now bear his name. There has since developed a popular concept that these eye lesions are a specific mark of vitamin A deficiency, and despite previously published evidence to the contrary, that idea often appears today. Bitot's spots are such easily recognized lesions that nutrition surveys may conveniently record their presence in large population studies. It is, therefore, important to appreciate the limitations of this conjunctival sign.

Part of the text of this paper is a synopsis of material submitted for publication elsewhere (1); some additional data obtained by McLaren in Tanganyika are also included. We have tried to present as briefly as possible the controversial status of Bitot's spots—particularly as this per-

tains to the interpretation of results of nutrition surveys.

Bitot's spots are grossly visible, discrete, and generally bilateral conjunctival changes—usually located temporally near the corneal limbus (see illustration). When large, they are typically triangular in shape, the apex pointing toward the outer canthus, although they exhibit considerable variation in size and configuration. Due to their foamy substance Bitot's spots have a characteristic refractile silvery-gray hue. If the foamy consistency is not pronounced they may appear as lusterless, finely striated plaques.

Occasionally individuals who do not show Bitot's spots may present identical material smeared along the lid margin or heaped at the outer canthus. Pinguecula, a lesion with a predilection for the same site on the bulbar conjunctiva as that of Bitot's spots, is a more common finding in any population and of no value as an indicator of nutritional deficiency. This lesion is yellowish or partially pigmented, and though elevated its substance lies beneath the epithelium. Moreover, it is less well demarcated and more solid in appearance than Bitot's spots and frequently occurs both nasally and temporally.

Neither pingueculae nor Bitot's spots produce symptoms, and in themselves they require no treatment. Pingueculae are found most commonly in adults, but in populations subject to exposure, they may occur with increased frequency in younger age groups. Bitot's spots

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are most often found in school-age children, with boys being more frequently affected than girls.

Bitot's spots rarely occur in well-fed populations but, instead, are customarily observed in areas where diet is restricted. They are not peculiar to the pigmented races. The possible etiological influences of race, hygiene, and climate are not easily appraised. Poor nutrition is a factor to be considered, but there is no single striking deficiency which consistently has been demonstrated to be a requisite for the appearance of Bitot's spots.

What is the evidence that Bitot's spots may be related to a lack of dietary vitamin A? Historically, the first suggestion comes from Bitot's description of these lesions in children with night blindness (2). Experimental studies since his time have specifically linked vitamin A deficiency to reversible night blindness. Impairment of night vision has not, however, been consistently related to Bitot's spots. Disappearance of the conjunctival spots with nutritional improvement and sometimes with vitamin A therapy alone has been reported (3-7). There is a single report of Bitot's spots occurring in experimental animals whose major deficiency was intended to be vitamin A (8).

On the other hand, experiments in human vitamin A deprivation have failed to produce these lesions (9), and there are several studies in which vitamin A administration or foods containing vitamin A failed to abolish Bitot's spots (10-15). In this group of publications night blindness was not presented as a characteristic accompaniment of the Bitot's spots, whereas most reports of favorable response to vitamin A have noted impaired night vision as a pretreatment condition.

Recently a mass survey of inhabitants of Ruanda-Urundi was performed for the appraisal of vitamin A deficiency as evidenced by Bitot's spots (16). Night vision was not tested. Although there was no correlation of blood levels of vitamin A with the presence or absence of Bitot's spots in individuals, there was a slightly lower average blood level of the vitamin for the total number of persons affected with the spots. Indeed, the observed levels of serum vitamin A were above those usually regarded as associated with clinically rec-

ognized deficiency states. Rather than proving a specific Bitot's spots-vitamin A correlation, the results might better be interpreted as indicative of a lower nutritional status in the group with conjunctival spots.

Histologically, Bitot's spots consist of masses of corynebacteria, keratinized epithelial cells, fatty debris, and edema of the mucosa and submucosa. None of these characteristics is pathologically specific for vitamin A deficiency. Bitot's spots contain no unique tissue characteristics. They are localized areas of xerosis whose appearance probably depends upon accumulation of bacteria on a site of bulbar conjunctiva which is relatively protected from lid massage.

Two terms traditionally associated with hypovitaminosis A are xerosis and keratomalacia. Full discussion of these terms extends beyond the scope of this paper, but their importance in regard to the significance of Bitot's spots warrants some mention.



**Typical Bitot's spot, a conjunctival lesion located temporally near the corneal limbus**

There is no satisfactory agreement as to how xerosis should be defined. Pathologically, it is a keratinizing metaplasia of the epithelium (17). Clinically, this gives the conjunctiva a dry, wrinkled, cadaverous appearance. The eyes of healthy persons who are subjected to prolonged outdoor exposure, such as sailors or farmers, may also attain the dry-eyed appearance with fine wrinkling of the bulbar conjunctiva. Such xerosis, or perhaps psuedoxerosis, does not attain the same severity, but it is also a

keratinization. These nutritionally normal people do not have Bitot's spots.

Conjunctival scrapings for the study of keratinized cells have not proved useful in detecting early changes from vitamin A deficiency, for the normal range in amount of keratinization is too great (18). Therefore, conjunctival xerosis as recorded in surveys should be regarded as a stage of keratinization which has become clinically manifest. From experimental work on hypovitaminosis, it is clear that this change in the epithelium can result from avitaminosis A, but to consider all clinical xerosis indicative of vitamin A deficiency would be incorrect. In contradistinction, keratomalacia, which is a rapid swelling and necrosis of the cornea found almost exclusively in infants, is a more specific evidence of vitamin A deficiency. Timely administration of vitamin A may produce a gratifying response.

Our own recent observations in Ethiopia and Tanganyika corroborate previous reports which have failed to show a correlation between vitamin A deficiency and Bitot's spots.

### Ethiopia

Seventeen hundred and ninety school children in Addis Ababa, Ethiopia, were examined for Bitot's spots in March 1959. Fifty-one were found to have the lesions, an incidence of 3.3 percent among the boys and 1.8 percent among the girls. The ages of the children examined varied over a wide range with an average of 12.3 years, about the same as the average age of those having Bitot's spots. Although the diet of these children was inadequate in several respects, general physical examinations performed on all those with Bitot's spots and a random sample of those without did not show gross

**Table 1. Serum vitamin A and carotene levels in school children with and without Bitot's spots, four examinations, Ethiopia, 1958-59**

Test item	Children with Bitot's spots				Children without Bitot's spots			
	School 1	School 2	School 3	Total	School 1	School 2	School 3	Total
<i>September 1958</i>								
Number of children.....	3	2	-----	5	28	11	12	51
Mean serum vitamin A (mcg./100 ml.).....	20.3	23.4	-----	21.5	23.8	20.2	25.8	23.4
Mean serum carotene (mcg./100 ml.).....	123.9	111.3	-----	118.9	129.8	103.4	152.3	129.4
<i>November 1958</i>								
Number of children.....	16	11	8	35	27	16	12	55
Mean serum vitamin A (mcg./100 ml.).....	24.0	22.8	28.5	24.7	23.4	29.0	25.7	25.5
Mean serum carotene (mcg./100 ml.).....	151.4	115.6	171.4	144.7	129.2	115.7	147.3	129.2
<i>March 1959</i>								
Number of children.....	12	12	8	32	27	10	8	45
Mean serum vitamin A (mcg./100 ml.).....	13.4	22.3	25.0	19.6	14.3	12.9	22.8	15.5
Mean serum carotene (mcg./100 ml.).....	125.9	154.0	184.0	150.9	154.9	179.1	150.4	159.5
<i>June 1959</i>								
Number of children.....	19	8	6	33	18	34	12	64
Mean serum vitamin A (mcg./100 ml.).....	19.4	25.5	20.7	20.9	20.6	28.4	18.7	25.7
Mean serum carotene (mcg./100 ml.).....	121.8	92.0	115.4	113.4	117.0	121.9	132.0	122.4

NOTE: School 1 children received skim milk and vitamin C; school 2 children, skim milk and vitamin A; school 3 children received no dietary supplements.

signs of specific deficiency disease. Compared with the bulbar conjunctivae of healthy American school children, the conjunctivae of all these Ethiopian children showed alterations, but the estimated severity of xerosis indicated by the degree of conjunctival wrinkling or dryness was not significantly different in the group with Bitot's spots from that in the group without the spots.

Night vision testing, using a modified radium plaque device (American Optical Instrument Co., U.S. Navy specifications), was performed, also in March 1959, on 244 of these Ethiopian children. Of this group, 28 had Bitot's spots

and 216 were without the spots. Standards for comparison were obtained by using the same instrument under comparable conditions to test a group of 77 American school children in Bethesda, Md. Based on these standards, no evidence of impaired night vision was found in any of the 244 Ethiopian children tested.

At three schools near Addis Ababa, serum carotene and vitamin A levels were determined on children with and without Bitot's spots in a series of four examinations (19). After the first examination children in school 2 (table 1) received supplements of 8,000 I.U. of vitamin A for 5 days per week for 6 weeks, whereas those

**Table 2. Observations of Bitot's spots in 10 patients at the Church Missionary Society Leprosarium, Makutapora, Tanganyika, in connection with vitamin A trial, 1959**

Patients		Observed state of lesions					
Sex	Age (years)	June 25, 1959	July 17, 1959	August 28, 1959	September 25, 1959	October 22, 1959	January 18, 1960
Female	40	Left lateral material approximately 3x3 mm. no definite shape, scattered foam	-----	No spot	-----	Few small spots again	Few small spots still present
Male <sup>1</sup>	20	Right lateral 6x3 mm. heavy accumulation	ISQ	-----	Very faint now. Left eye now has faint striations	Right eye and left eye ISQ	Large amount of material lateral and bilateral
Female <sup>1</sup>	25	Right lateral patch of foam on a larger white area	ISQ	Much diminished	No further change	Still present	ISQ but only raised, no foam
Male	29	Left lateral dumbbell-like area of material	-----	No spot	-----	Returned and increased	Still larger
Male <sup>1</sup>	8	Right lateral two flecks of foam only	No spots	One small fleck	-----	-----	ISQ
Male <sup>1</sup>	40	Right medial three small areas on pinguecula	Doubtful if present	Definitely present again	-----	ISQ	ISQ
Male <sup>1</sup>	26	Left lateral two definite spots	ISQ	Complete disappearance	-----	-----	Two large spots, no foam
Male <sup>1</sup>	30	Left medial one small spot	-----	Minute	Nothing seen	Spot returned	Left lepro-sarium
Male	30	Left lateral pinhead spot	-----	Nothing seen	Small spot seen	Small spot, both eyes laterally	ISQ
Male	40	Left lateral appreciable size	ISQ	Left lepro-sarium	-----	-----	-----

<sup>1</sup> Patients receiving vitamin A therapy.  
ISQ=In status quo.

**Table 3. Percent incidence of Bitot's spots, xerophthalmia, and keratomalacia among children examined in Tanganyika, March 1959**

Item	Mvumi		Mwanza	
	Male	Female	Male	Female
<i>School children</i>				
Number examined.....	670	395	331	114
Percent incidence:				
Bitot's spots.....	0.4	0.5	1.8	0
Xerophthalmia.....	0.3	0.2	0	0
<i>Preschool children</i>				
Number examined.....	232	236	-----	-----
Percent incidence:				
Bitot's spots.....	0	0	-----	-----
Xerophthalmia.....	8.2	5.5	-----	-----
Keratomalacia.....	1.7	0.8	-----	-----

in the other two schools did not. Eight weeks after the second examination supplementation was discontinued. Supplementation was resumed after the third examinations. The distribution of levels of serum vitamin A and carotene in individuals with Bitot's spots followed the same pattern found throughout the country in the initial survey of over 8,000 persons.

This relatively short-term study has failed to reveal any effect on Bitot's spots from vitamin A administration.

### Tanganyika

Subsequent to our work in Ethiopia, further observations of Bitot's spots in relation to vitamin A were made on a smaller scale in Tanganyika.

A trial of vitamin A therapy, supervised by Dr. K. R. Dalley, was undertaken with a few patients at the Church Missionary Society Leprosarium at Makutupora in 1959. Ten patients with Bitot's spots were divided into two groups for treatment and observation. During the trial period, June 25–October 14, six patients received 150,000 I.U. of vitamin A twice weekly under the supervision of a European nurse. Four patients received no vitamin A supplement.

The Bitot's spots of patients in both groups

were observed several times during the trial and again 3 months after vitamin A therapy had been stopped (table 2). Though the conjunctival lesions varied considerably from one observation period to another (similar variations occurred in the individual Ethiopian school children with Bitot's spots during the 9 months of observation), there was no difference in the pattern of variation in individuals treated with vitamin A as compared with those untreated. Nor did vitamin A blood levels show differences between the two groups. The night vision of seven of the patients showed no impairment.

In Mwanza, Tanganyika, on the shores of Lake Victoria, there is no food shortage. At Mvumi, Tanganyika, in the dry central Province where famine has been frequent, there is dietary deficiency of vitamin A and protein. The occurrence of Bitot's spots among school children in these two areas was 5 cases in 1,065 children examined in Mvumi and 6 cases in 445 children examined in Mwanza—at least as many spots in Mwanza as in the nutritionally less fortunate region (table 3). Among 468 preschool children in Mvumi, keratomalacia had occurred in 6, whereas in Mwanza during 2 years of pediatric, ophthalmic, and nutritional hospital practice, not a single case has been discovered. In Addis Ababa, for another example, keratomalacia is said to be rare. No case was seen during the nutrition survey of Ethiopia in 1958 (19). Therefore, keratomalacia, the more specific indicator of vitamin A deficiency, and Bitot's spots are not necessarily associated occurrences.

This conclusion is worthy of emphasis. There need be no correlation between the presence of Bitot's spots and hypovitaminosis A. For this reason, the convenience of recording Bitot's spots in nutritional surveys must not tempt workers into assigning a specific interpretation to these lesions. Like other clinical signs, the nutritional significance of the lesion must be evaluated in conjunction with other evidence.

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